THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SAVAS ANASTASSIADIS, ALEXANDER AIVASIDIS and CHRISTIAN WANDREY

Application No. 08/208,123

ON BRIEF

Before WILLIAM F. SMITH, SPIEGEL and MILLS, <u>Administrative Patent Judges</u>, MILLS, <u>Administrative Patent Judge</u>.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 3, 6-9, 11 and 13-21, which are all of the claims pending in this application.

We reverse.

Claim 21 is illustrative of the claims on appeal and reads as follows:

- 21. A process for the continuous production of citrate or citric acid, comprising the steps of:
- (a) continuously feeding to a fermenter containing a yeast of the genus Candida capable of transforming glucose to citric acid by fermentation and a nutrient medium, oxygen, a carbon source selected from the group consisting of glucose, saccharose, molasses and hydrolysates of starch which are convertible by candida strains to citric acid, and at least one ammonium compound as a nitrogen source, to obtain a fermentation medium containing the carbon source in a concentration corresponding to 200 to 400 g/l of glucose;
- (b) fermenting the carbon source in the fermentation medium to citric acid in said fermenter at a temperature of about 29 to 31°C, a pH of 4 to 5.5 and for a mean residence time of 60 to 120 hours, while controlling the carbon/nitrogen ratio of the carbon source and the nitrogen source fed to said fermenter to correspond to a molar ratio of 12 to 22 parts carbon source taken as glucose per part nitrogen source, taken as NH₃, and controlling an oxygen concentration in said fermenter to corresponding to 15 to 30% of air oxygen saturation of said medium^[1];
 - (c) continuously withdrawing fermentation product from said fermenter; and
 - (d) recovering citrate or citric acid from said fermentation product.

The prior art reference of record relied upon by the examiner in rejecting the appealed claims is

Takayama et al (Takayama) 4,322,498 Mar. 30, 1982

¹ This step is interpreted to mean controlling the amount of oxygen contained in the fermentation medium as a percentage of the total amount of oxygen which could be held by said fermentation medium. See Paper No. 7, page 4, filed May 19, 1995.

A prior art reference relied on by appellants (Brief, pages 8-9) is:

Klasson et al. (Klasson), "Continuous Fermentation for the Production of Acid from Glucose," Applied Biochem. Biotech., Vol. 20/2189, pages 491-509 (1989).²

OPINION

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, to the applied prior art references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the above-noted rejection, we make reference to the Examiner's Answer (Paper No.13, mailed October 2, 1995) for the examiner's complete reasoning in support of the rejection, and to the appellants' Brief (Paper No. 11, filed July 21, 1995) and Supplement to Appeal Brief (Paper No. 16, filed January 26, 1999) for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

² Klasson was made of record in the Information Disclosure Statement filed March 8, 1994, (Paper No. 3).

Issue³

Claims 3, 6-9, 11 and 13-21 stand rejected under 35 U.S.C. § 103. The examiner relies on Takayama as evidence of obviousness of the rejected claims. We agree with the examiner's rejection in view of the disclosure of Takayama up to a point. Takayama does disclose the production of citric acid using Candida yeast strains similar to those of the present invention in the presence of glucose as a carbon source, ammonium as a nitrogen source, and under aerobic conditions (conditions requiring oxygen). The examiner acknowledges that Takayama does not disclose the exact nutrient ratios which are now claimed.

It is the examiner's position that a skilled artisan is always motivated to adjust the concentrations of nutrients in order to maximize production and can do so as a matter of routine experimentation. Examiner's Answer, unnumbered page following first numbered page 3. The examiner further submits that altering one or both of oxygen or glucose levels in order to optimize the production of citrate would be a matter of routine experimentation. Examiner's Answer, second numbered page 3.

³ The examiner has withdrawn the final rejection of the appealed claims under 35 U.S.C. § 112, second paragraph, as claim 21 being indefinite (see Examiner's Answer, page 2).

We cannot agree with the examiner that the claimed ratios and ranges were the result of routine experimentation, and in our judgment, any such experimentation would not have come from within the teachings of the applied art.

Takayama discloses a batch process⁴ for preparing citric acid in which glucose levels as high as 150 g/L (as sugar) of invertase treated blackstrap molasses (Column 9, line 38, Example 8) may be used. In the batch process of Takayama, the culturing step is generally carried out under aerobic conditions (Column 4, lines 42-45).

The claimed continuous process of producing citric acid requires process steps of "controlling the oxygen concentration to correspond to 15 to 30% of air oxygen saturation of said medium;" of "obtaining a fermentation medium containing the carbon source in a concentration corresponding to 200 to 400 g/l of glucose;" and "controlling the carbon/nitrogen ratio of the carbon source and the nitrogen source fed to said fermenter to correspond to a molar ratio of 12 to 22 parts carbon source taken as glucose per part nitrogen source, taken as NH₃." The criticality of the oxygen saturation values to the claimed process, in particular, is reasonably established by the production data in Figure

⁴ The examiner recognizes that Takayama discloses a batch process, not a continuous process as claimed, and argues that conversion of a fermentation to a continuous culture is notoriously old and well known in the art. Examiner's Answer, second numbered page 3. However, "P.E. Milsom," Food Biotechnology Vol. I, p. 291 (1987), which is cited in the specification at page 3, acknowledges art recognized difficulties in conversion of a citric acid production process from a batch process to a continuous process. This fact remains unaddressed by the examiner.

3 of the application. <u>In re Waymouth</u>, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974).

In our view, Takayama does not provide sufficient reasoning to select or suggest the claimed variables and their use in combination in a continuous process, as claimed. Although it is the examiner's position that optimization of these variables is within the skill of the art, it is well settled that such optimization or "obvious to try" is not the correct standard for determining obviousness under 35 U.S.C. § 103. See In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

In the present case, the examiner has not even established that the claimed parameters for carbon source concentration, carbon/nitrogen ratio and oxygen saturation, are within the ranges for the variables disclosed in Takayama. We find it significant that the specifically claimed ranges for glucose and oxygen saturation in the continuous process for the production of citric acid claimed, fall outside the indicated optimum values for glucose and aerobic conditions (oxygen requirement) disclosed in the batch process of Takayama. See In re Sebek, 465 F.2d 904, 907, 175 USPQ 93, 95 (CCPA 1972). Incidentally, it was determined in Sebek that in "an area of technology shown to be highly unpredictable in process values, the discovery of optimum values not in any way

suggested by the prior art is more likely to be unobvious than obvious within the meaning of § 103." See In re Sebek, 465 F.2d 904, 907, 175 USPQ 93, 95 (CCPA 1972).⁵

In rejecting claims under 35 U.S.C. § 103, it is incumbent upon the examiner to establish a factual basis to support the legal conclusion of obviousness. See In re Fine, 837 F.2d 1071, 1073, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). In so doing, the examiner is expected to make the factual determinations set forth in Graham v. John Deere Co., 383 U.S. 1, 17, 148 USPQ 459, 467 (CCPA 1966), and to provide a reason why one having ordinary skill in the pertinent art would have been led to modify the prior art to arrive at the claimed invention. Such reason must stem from some teaching, suggestion or implication in the prior art as a whole or knowledge generally available to one having ordinary skill in the art. Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F.2d 1044, 1051, 5 USPQ2d 1434, 1438 (Fed. Cir.), cert. denied, 488 U.S. 825 (1988); Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 293, 227 USPQ 657, 664 (Fed. Cir.), cert. denied, 475 U.S. 1017 (1986); ACS Hosp. System., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). These showings by the examiner are an essential part of complying with the burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

⁵ See footnote 2.

All the claims under appeal require process steps of "controlling the oxygen concentration to correspond to 15 to 30% of air oxygen saturation of said medium" and of "obtaining a fermentation medium containing the carbon source in a concentration corresponding to 200 to 400 g/l of glucose." The claims also require a specific ratio of carbon source to nitrogen. These claim limitations and their use in combination, are not suggested by Takayama. The examiner does not provide reasons, motivation or a suggestion for modifying the batch process of Takayama or for selecting the specific claimed process requirements, or their resulting citric acid production advantages.

To supply these omissions in the teachings of the applied prior art, the examiner made determinations that these differences would have been obvious to an artisan who would alter one or both variables in order to optimize the production of citrate and would be a matter of routine experimentation. Examiner's Answer, second numbered page 3. However, what is missing from the examiner's analysis is evidentiary support that would have led an artisan to select variables outside or in addition to those set forth in Takayama to arrive at the claimed invention. In our view, the only reason or suggestion for modifying the batch process of Takayama for producing citric acid as set forth in the manner proposed by the examiner to meet the above-noted claim limitation, stems from hindsight knowledge derived from the appellants' own disclosure. The use of such hindsight knowledge to support an obviousness rejection under 35 U.S.C. § 103 is, of course,

impermissible. See, for example, W. L. Gore and Assocs. Inc. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). The examiner may not resort to speculation, unfounded assumption or hindsight reconstruction to supply deficiencies in the factual basis for the rejection. See In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968).

Similarly, the examiner argues that the slight difference in [production] results described in the specification and Fig. 3 would appear to be no more than a difference of degree rather than a difference in kind (Examiner's Answer, page 4). In In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), a predecessor of our appellate reviewing court set out the rule that the discovery of an optimum value of a variable in a known process is normally obvious. Exceptions to this rule have been found in cases where the results of optimizing a variable, which was known to be result effective, were unexpectedly good. In re Waymouth, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974). Another exception is the case in which the parameter optimized was not recognized to be a result-effective variable. See In re Antonie, 559 F.2d 618, 619, 195 USPQ 6, 8 CCPA 1977). In the present case, the result of obtaining increased citric acid production in a continuous process by selecting a combination of parameters including air saturation of the medium coupled with a specific glucose requirement and

glucose/nitrogen ratio, when taken together, are not reasonably suggested or recognized to be "result effective" by Takayama.

In our view, the examiner has not furnished an adequate evidentiary foundation from which a conclusion of obviousness can be reached. It follows that we cannot sustain the examiner's rejections of claims 3, 6-9, 11 and 13-21.

CONCLUSION

The decision of the examiner to reject Claims 3, 6-9, 11 and 13-21 under 35 U.S.C. § 103 is reversed.

REVERSED.

WILLIAM F. SMITH Administrative Patent Judge))
))) BOARD OF PATENT
CAROL A. SPIEGEL Administrative Patent Judge) APPEALS AND
)) INTERFERENCES)
DEMETRA J. MILLS Administrative Patent Judge))

Appeal No. 1996-2214 Application No. 08/208,123

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